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| 09/991,445      | 11/16/2001  | Ernest G. Schutt     | ALLIA.62F1C1C1      | 3983             |

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EXAMINER

SHARAREH, SHAHNAM J

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1617

DATE MAILED: 10/22/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/991,445

Applicant(s)

SCHUTT ET AL.

Examiner

Shahnam Sharareh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11/16/2001, 7/31/03.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 8, 11 and 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9, 10, 12-15 and 17-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

1. Claims 1-20 are pending. Applicant's election of species set forth in Paper No. 6 is acknowledged. Accordingly, perfluorobutane is elected as the species for fluorocarbons and oxygen is elected as the species for the modifier gas. Claims 1-7, 9-10, 12-15, 17-20 read on the elected species. Claims 8, 11, 16 are withdrawn from further consideration as they are not directed to elected species.

Applicant's traversal has been considered but has not been found persuasive. Applicant argues that other published patents were issued with no election of species requirement. As the initial matter, published patents are intellectual properties, not legal precedents. Second, each patent application is prosecuted on its own merits. Therefore, Applicant's conclusion is not persuasive.

Applicant further argues that it is not clear why claim 1-20 are generic. Applicant specifically states, what are Markush claims 9, 14, 20 generic to? In response Examiner states, the fact that applicant has elected a species of fluorocarbon and a modifier gas is an indication that the election requirement was sufficiently clear for applicant to make an election. Therefore, such argument is moot on its face.

Further, in response to Applicant assertion about unity of invention, Examiner states that Applicant appears to be confusing the Unity of Invention Requirement under PCT treaty with U.S. requirement under 35 USC 121 which follows a different standard.

Applicant finally states that there is no procedural requirement for Applicant to traverse the requirement and goes on record and admit that all of the various fluorocarbon species are obvious variants. In response, Examiner states that Applicant

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appears to have simply misunderstood the statement on the election requirement. The requirement states "Should applicant traverse on the ground that the species are not patentably distinct, then applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants" of each other. Accordingly, the traversal must be on the basis that "species are not patentably distinct," for the requested admission to be of probative value. Indeed, if the species are claimed "not to be patentable distinct," it would flow logically with such traversal that they are obvious variants of each other. In either scenario, the requirement does not strip applicants right from examination of the entire scope, so long as, it is consistent with the requirement set forth by 35 USC 121. In the instant case, Examiner has declared various gases in the genus of fluorocarbon gas to be patentably distinct. For example, perfluorotriethylamines do not exist in gaseous state at room temperature, but perfluoropropane does. Thus, these two fluorocarbons are chemically and physically different, and are viewed to be patentably distinct; and essentially not obvious variants. For such reasons, Applicant's arguments are not found persuasive and the election of species is proper.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

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patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-7, 9-10, 12-15, 17-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of 1-12 of US Patent 6,372,195, claims 1-101 of US Patent 6,258,339, claims 1-24 of US Patent 5,695,741, claims 1-38 of US Patent 5,639,443, and claims 17-22 of US Patent 5,798,091, claims 1-9, 38-73 of US Patent 5,804,162, claims 26-51 of US Patent 6,193,952.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant methods are drawn to the use of specific perfluorocarbon gases and a secondary modifier gas. The patented claims are also directed to microbubbles comprising at least a perfluorocarbon and a secondary nonperfluorocarbon gas. Thus, the patented claims meets all elements of the instant claims and anticipate the pending claims. Therefore, the instant claims are subject to a double patenting rejection.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
  2. Ascertaining the differences between the prior art and the claims at issue.
  3. Resolving the level of ordinary skill in the pertinent art.
  4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
3. Claims 1-6, 9-10, 13-15, 17-18, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider et al US Patent 5,413,774 in view of Tickner US Patent 4,265,251.

The instant claims are directed to microbubbles comprising a perfluorobutane gas and a nonfluorocarbon secondary gas.

Schneider teaches gas filled microvesicles that can contain mixture of a first perfluorocarbon gas such as perfluorobutane (C<sub>4</sub>F<sub>10</sub>) and a secondary gas such as air which contains oxygen, nitrogen, CO<sub>2</sub> and the like. (see col 5, lines 50-56; examples 7-8; claims 1-2, col 14, lines 45, 68). Schneider also teaches a membrane around his microvesicles (see claims 5-9). Schneider's fluorocarbon is the same as those instantly claimed; therefore, is inherently possesses the same functional characteristics as the instant fluorocarbon. Air, nitrogen and the like gases also fall within the instant genus of modifier gases. Schneider fails to specifically use oxygen in his gaseous mixture.

Tickner teaches methods of ultrasound imaging using gas containing microbubbles (abstract, col 7, lines 11-54). Tickner teaches that although the preferred gas is carbon dioxide, however, other gases such as freons and oxygen may be used in

his contrast agents (col 6, lines 63-67). Tickner fails to specifically teach the use of perfluorobutane in his compositions for ultrasound imaging.

Although Schneider fails to use oxygen with pefluorobutane in his gaseous mixtures compositions, he specifically teaches that any gas like air and nitrogen can be employed in his gaseous mixture. Tickner shows that for the purposes of ultrasonic contrast agents, gases such as oxygen, nitrogen, and Freons are substantially interchangeable and are functional equivalents. Thus, absence of showing unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to substitute one of air or nitrogen gases in Schneider's microvesicles with oxygen and create a microvesicle tha contains pefluorobutane and oxygen, because as shown by Tickner, oxygen is considered art recognized equivalents to suitable gases enumerated by Schneider. Subsequently, the ordinary skill in the art would have had a reasonable expectation of success in mixing perfluorobutane with oxygen to produce a gaseous microvesicles.

4. Claims 1-6, 9-10, 13-15, 17-18, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider in view of Unger US Patent 5,205,290.

The teachings of Schneider are described above. Schnedder does not specifically uses oxygen in his gaseous mixture.

Unger teaches contrast agents comprising gaseous microspheres containing oxygen. (see abstract; col 5, lines 10-25, claim 8). Unger also teaches the use of volatile liquids having low boiling points within his microspheres to allow expansion of the microspheres (see col 4, lines 9-58). Unger specifically teaches the use of

perfluorocarbons such as those having between 1 and about 9 carbon atoms especially  $C_4F_{10}$  (perfluorobutane). Accordingly, Unger teaches the *in vivo* administration of oxygen and perfluorobutane as gas expanding compounds within the microspheres of his contrast agents. Unger, however, fails to use his compositions for ultrasound imaging.

Nevertheless, it would have been obvious to one of ordinary skill in the art at the time of invention to utilize a mixture of a suitable perfluorocarbons such as perfluorobutane, as taught by Schneider, and oxygen, as taught by Unger, because the ordinary skill in the art would have had a reasonable expectation of success in preparing a gaseous microbubble for therapeutic or diagnostic use. Absence of showing unexpected results, one of ordinary skill in the art would have had a reasonable expectation in observing similar properties when mixing perfluorobutane of Schneider with oxygen of Unger for use ultrasound imaging.

### ***Conclusion***


No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 703-308-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.



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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.



Shahnam Sharareh, PharmD  
Patent Examiner, AU 1617

ss  
10/15/03